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Original Article

Serum lipoprotein (a) in diabetic patients with various renal function not yet on dialysis

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ABSTRACT

To examine the association of serum serum lipoprotein(a)[Lp(a)] concentration with various demographic and biochemical indexes of diabetic patients , we conducted a study on type 2 diabetes mellitus(T2D) patients. Patients were under treatment with insulin injection or oral hypoglycemic agents with various creatinine clearances not yet on dialysis. We studied 122 patients, with a mean age of 63 ± 10 years .The duration of diabetes was 7.4 ± 5.8 years. In this cross-sectional study, serum Lp(a), HbA_{1c} , body mass index (BMI) and creatinine clearance were assessed. The mean serum Lp(a) was 22.2 ± 24.7 mg/dL (median: 18.3 mg/dL), and serum Lp(a) levels more than 30 mg/dL was found in 29 (23.8%) patients. A significant inverse correlation of serum Lp(a) with clearance of creatinine was observed. This study suggests that renal function is an independent determinant of serum Lp(a) in diabetic patients.

KEY WORDS: Lipoprotein(a), Diabetes mellitus, Creatinine clearance.

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INTRODUCTION

Lipoprotein(a) [Lp(a)], is a macromolecule which consists of a glycoprotein apolipoprotein(a), which is disulfide linked to apolipoprotein B-100 on an LDL core.[1-6] Its concentrations are primarily genetically determined[7-12], and various studies have shown that, high levels of Lp(a) in plasma, is an independent risk factor for premature atherosclerotic coronary artery disease.[10-16] The normal metabolism and the role and of this lipoprotein are not fully elucidated.[14-21] Several studies have shown, high concentrations of Lp(a) in diabetic patients, which has led to speculation that Lp(a) may contribute to the greatly increased incidence of vascular disease associated with diabetes.[4,21] However, considerable debate still remains, regarding the precise value of serum Lp(a) levels in type 2 diabetes(T2D) patients. In non-diabetic patients, renal disease correlates with elevated levels of Lp(a) that are normalized by kidney transplantation.[2,16,18,20] Kidney involvement is a frequent complication of diabetes that has prompted speculation that, kidney dysfunction is the principal cause of raised Lp(a) in T2D patients.[2-7] This study aimed to investigate the association of serum Lp(a) level with various indexes of demographic and biochemical of T2D patients.

METHODOLOGY

Patients: This cross-sectional study was conducted on a group of T2D patients who were admitted in the hospital for controlling the diabetes with either insulin injection or oral hypoglycemic

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agents. Exclusion criteria included presence of any infections and use of lipid-lowering medications. All patients signed consent forms for participation in this study.

Laboratory tests: After admission to hospital, detailed medical history was obtained, and careful physical exam was performed. Serum Lp(a) were measured by enzyme-linked immunosorbent assay kit (Macra® Lp(a) manufactured by Strategic Diagnostics Inc. for Trinity Biotech USA, Jamestown, NY, USA). Results were expressed in mg/dL; the intra- and inter assay coefficients of variation for this method were < 5% and < 10%, respectively. Serum Lp(a) levels of 30 mg/dL was considered as the threshold value of risk for its pathological effect. Serum glycosilated hemoglobine (HbA_{1c}) was measured by chromatography method using Hb-Gold of UK; normal level in our laboratory is up to 6.1%. Levels of serum albumin (Alb), serum creatinine (Cr), blood urea nitrogen (BUN) total protein, triglyceride (TG), cholestrol (chol), and high density lipoprotein (HDL-C) were measured using standard methods. Body mass index (BMI) was assessed using the standard formula.[22] Serum LDL-C was calculated by friedewald's formula.[23] Creatinine clearance was evaluated from serum creatinine, age and body weight.[24]

Statistical analysis: Data are expressed as the mean ± SD and median values. For correlations we used the partial correlation test. For comparison between females and males student's ***t*** test was used. To normalize of the serum Lp(a) data, the cube root of Lp(a) was assessed and used. All analyses were performed with the SPSS statistical package (version 11.0 for Windows; SPSS, Chicago). Statistical significance was determined at value of $p < 0.05$.

RESULTS

In Table-I the baseline characteristics of the study patients are shown. One hundred twenty two patients (40 males, 82 females) with a mean age of 63 ± 10 years, was enrolled to this study. The mean duration of diabetes were 7.4 ± 5.8 years (median: 6 years). The mean serum Lp(a) was 22.2 ± 24.7 mg/dl (median: 18.3 mg/dl). Serum Lp(a) levels > 30 mg/dl was found in 29 patients (23.8%). The mean of creatinine clearance was 64± 24. We found a significant inverse correlation of duration of diabetes mellitus (DM) with creatinine clearance ($r = -0.51$, $p < 0.001$).A significant inverse correlation of serum Lp(a) with creatinine clearance ($r = -0.19$, $p = 0.03$) was seen. We did not find a significant correlation of serum Lp(a) with age, or DM, BMI, serum Alb, total protein, lipids or serum HgA_{1C}.

DISCUSSION

Our results demonstrated a significant inverse correlation of duration of DM and serum Lp(a) with creatinine clearance. There was no significant correlation of serum Lp(a) with age, BMI, serum Alb, total proteins, lipids and serum HgA1c. Serum Lp(a) levels > 30 mg/dl was found in 23.8% of patients. Recent studies suggest that Lp(a) can act as a marker for determining vascular or tissue injury.[25]

Table-I: Patients' data and laboratory tests of the 122 study patients.

Parameters	*Minimum*	*Maximum*	*Mean±SD*	*Median*
Age (years)	25	84	63±11	64
Duration of DM (years)	0.1	25	7.4±6.8	6
BMI (kg/m2)	30	53	25.5±4.5	25.3
Systolic blood pressure (mmHg)	100	180	138±23	80
Diastolic blood pressure (mmHg)	50	130	83±12	140
Creatinine clearance (ml/min)	10	110	64±24	64
Lipoprotein(a) (mg/dl)	0.10	134	22.2±24.8	18.3
Albumin (g/dl)	2.5	7.5	4.9±1	4.9
Total protein (g/dl)	5	12.5	7.2±0.9	7
HgbA1C %	3.9	13.5	7.6±1.9	7.6
Cholestrol (mg/dl)	90	38.8	198±52	192
Triglyceride (mg/dl)	37	580	183±102	155
LDL-C (mg/dl)	44	210	112±37	112
HDL-C (mg/dl)	19	128	47±18	44

Recent findings have also demonstrated that Lp(a) is an independent risk factor for the progression of diabetic nephropathy in T2D patients.[26,27] Indeed macroalbuminuria was associated with raised plasma Lp(a) regardless of the marker used to identify kidney failure.[28-42] Moreover, altered kidney function, is a major determinant of raised Lp(a) levels in microalbuminuric and normoalbuminuric diabetics patients.[34,35] Increase in plasma Lp(a) levels was seen in various studies in nondiabetics.[34-42] Increased levels of Lp(a) is an independent risk factor for vascular disease in the general population and in diabetic patients.[43-54] In view of these findings, defining the relationship between renal complications and levels of serum Lp(a) in diabetic patients is mandatory.

CONCLUSION

Our results suggest that serum Lp(a) concentration was associated with clearance of creatinine as a primary determinant of raised serum Lp(a) in diabetic patients. This has important implications for the increased susceptibility to vascular disease associated with Lp(a) in diabetic patients.

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